

REVIEW ARTICLES

Richard P. Cambria, MD, Section Editor
From the Canadian Society for Vascular Surgery

Mortality and reintervention following elective abdominal aortic aneurysm repair

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Background: The objective of this study is to provide an up-to-date meta-analysis on the short- and long-term mortality rates of elective repair of abdominal aortic aneurysms (AAAs) via the open and endovascular approaches.

Methods: MEDLINE, EMBASE, and Cochrane Central Register of Controlled trials, conference proceeding from major vascular meetings were searched for randomized trials comparing open vs elective endovascular aneurysm repair (EVAR) of AAAs. A random-effects model was used for analysis. Risk ratio (RR) and 95% confidence intervals (CIs) of open vs EVAR were calculated for short- and long-term mortality and reintervention rates.

Results: The analysis encompassed four randomized controlled trials with a total of 2783 patients. The open repair group resulted in significantly increased 30-day postoperative all-cause mortality compared with EVAR repair group (3.2% vs 1.2%; RR, 2.81; 95% CI, 1.60-4.94); however, there is no statistical difference in the long-term all-cause mortality between both groups (RR, 0.97; 95% CI, 0.86-1.10). Interestingly, fewer patients underwent reintervention procedures in the open repair group compared with those who had EVAR repair (9.3% vs 18.9%; RR, 0.49; 95% CI, 0.40-0.60), but this finding is doubtful due to the large heterogeneity. Lastly, no statistical difference in long-term mortality rates attributable to cardiovascular disease (CVD), aneurysm related, or stroke were found between the two types of repair.

Conclusions: Results of this meta-analysis demonstrate that the 30-day all-cause mortality rate is higher with open than with EVAR repair; however, there is no statistical difference in the long-term all-cause and cause-specific mortality between both groups. The reintervention rate attributable to procedural complication was higher in the EVAR group. Because of the equivalency of long-term outcomes and the short-term benefits of EVAR, an endovascular-first approach to AAAs can be supported by the meta-analysis. (*J Vasc Surg* 2013;57:1676-83.)

As a frequent cause of cardiovascular mortality, abdominal aortic aneurysms (AAAs) place a significant burden on health care systems in developed nations.^{1,2} Recent studies have shown a prevalence of AAA as high as 9% in people 65-85 years of age.² The risk of rupture, which is fatal in 65% of individuals, is directly correlated with the aneurysm's diameter.³ Surgical intervention is currently the accepted standard used to prevent mortality from aneurysm rupture. This can be approached from either a standard

open technique or an endovascular procedure with a stent graft system. The open approach, practiced by surgeons for over 50 years, had been the treatment of choice until a less invasive alternative, endovascular aneurysm repair (EVAR), was developed.⁴ With similar indications for both approaches, deciding on an elective repair method can be very challenging. Several trials have compared the EVAR and open approaches, focusing on their effectiveness and outcomes. However, there are still some controversies in the literature on the short- and long-term mortality rates of these approaches.² Our goal is to review the current evidence comparing the open and EVAR approaches for AAA repair by performing a meta-analysis of all the randomized controlled trials that compared both approaches with regard to their effectiveness and safety.

METHODS

Design. A systematic review and meta-analysis of randomized clinical trials were conducted.

Outcome of interest. The primary outcome of interest was short- and long-term all-cause mortality. We considered mortality within 30 days after the operation to represent the short-term mortality rate, whereas mortality

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Table I. Description of the included trials (RCTs)

Source	Age, mean \pm SD, years		Number of patients		Inclusion criteria	Key exclusion criteria	Follow-up duration
	Open	EVAR	Open	EVAR			
ACE 2011 ¹	70 \pm 7.1	68.9 \pm 7.7	148	150	(1) CT scan finding: AAA >50 mm in men, >45 mm in women, common iliac artery aneurysm >30 mm (2) Upper neck free of major thrombus or calcification (3) \geq 15 mm in length (4) Angle between neck and axis of aneurysm <60 mm (5) Clinical assessment graded patients in categories of 0-2 according to comorbidity score of SVS/AAVS	(1) Previous AAA surgery (2) Ruptured aneurysm (3) Mycotic aneurysm (4) Severe iodine allergy (5) Life expectancy deemed <6 months (6) Category 3 of SVS/AAVS	4.8 years
DREAM 2010 ¹⁴	69.6 \pm 6.8	70.7 \pm 6.6	178	173	(1) Elective repair (2) AAA size >5 cm (3) Suitable for operation as per cardiology/inter-nist for open and endograft-dependent anatomic criteria for EVAR	(1) Emergency repair (2) Inflammatory aneurysm (3) Anatomic variation (4) Connective tissue disease (5) History of organ transplant (6) Life expectancy less than 2 years	6.4 years
EVAR I ¹² 2011	74.1 \pm 6.1	74.1 \pm 6.1	626	626	(1) Elective repair (2) AAA >5.5 cm (3) Surgical candidate (4) Age >60 years	NA	8 years
OVER ¹⁵ 2009	70.5 \pm 7.8	69.6 \pm 7.8	437	444	(1) Elective repair (2) AAA >5 cm (3) AAA of 4.5 cm and a rapidly enlarging aneurysm (4) Surgical candidate (5) An associated iliac aneurysm with a maximum diameter of at least 3 cm	(1) Previous abdominal aortic surgery (2) Needed urgent report. Unwilling or unable to give informed consent or follow the protocol	2 years

AAVS, American Association for Vascular Surgery; AAA, abdominal aortic aneurysm; ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR I, United Kingdom Endovascular Aneurysm Repair I; NA, not available; OVER, Open Versus Endovascular Repair; RCT, randomized controlled trial; SVS, Society for Vascular Surgery.

beyond the 2-year mark was considered to represent the long-term mortality rate. Secondary outcomes of interest included cardiovascular-related death, aneurysm-related death, and reintervention rates.

Criteria for study selection. All randomized controlled trials comparing the mortality rates of EVAR

vs open AAA repair were included. Study selection included randomized controlled trials (RCTs) published until 2012 that (1) enrolled patients for elective repair of AAAs with a size \geq 5 cm or AAAs of 4.5 cm that are rapidly enlarging; (2) all patients were good surgical candidates; and (3) the studies reported all-cause mortality

(short-term/long-term), aneurysm-related mortality, cardiovascular disease (CVD)-related mortality (including congestive heart failure, myocardial infarction, cardiac arrest), stroke-related mortality, and surgical reintervention rates. We excluded RCTs that had (1) patients with previous abdominal aortic surgery; (2) patients who needed urgent surgery for ruptured AAAs; (3) patients unwilling or unable to give informed consent or follow the protocol; and (4) studies with a mean follow-up of less than 2 years.

Literature search and study selection. Studies were identified by electronic literature searches in the Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE from 1988 to 2012 using combinations of the following terms: aortic graft, endovascular, EVAR, open, abdominal aortic aneurysm, AAA, and repair. We also contacted trials' authors for further data as needed. Our literature search also included reviewing the references of recent articles published on this topic including the issues from the past 12 months of the *Journal of Vascular Surgery*. All available data were utilized including full publications, abstracts, and online late breaking presentations. We identified 2245 reports that were reviewed by two independent reviewers (M.Q., F.P.); a third reviewer (T.R.) settled any discrepancies. A previous meta-analysis was published on this topic; however, this meta-analysis does not include the results from the most recent RCTs.⁵ We also did an analysis of a number of prospective RCTs but did not include these in our meta-analysis as per the inclusion criteria.

Data collection. Two authors (M.Q., F.P.) independently identified the trials for inclusion and exclusion criteria as mentioned above. For all published trials, the following information was tabulated according to the randomization group by two authors (M.Q., F.P.): (1) information about the trial's clinical characteristics, the number of participating patients, mean age, and duration of clinical follow-up (Table 1); and (2) aneurysm related mortality, CVD related mortality (including congestive heart failure, myocardial infarction, cardiac arrest), stroke related mortality, surgical reintervention rates, short-term all-cause mortality (<30 days) and long-term mortality (>2 years with short-term deaths excluded). If no resolution of agreement was achieved between the reviewers, a senior author (T.R.) was consulted to settle the discrepancy. The level of agreement between the two authors (M.Q., F.P.) varied from 83% to 100%.

Assessment of quality and risk of bias. The risk of bias was assessed according to the guidelines of The Cochrane Collaboration tool for assessing risk of bias.⁶⁻¹¹ The assessment of risk of bias in the trials was based on consequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias such as baseline imbalance, early stopping bias, academic bias, and source of funding bias.⁶ M.Q. and F.P. assessed the risk of bias in all trials with a third reviewer (T.R.) to settle any discrepancies.

Statistical analysis. The reliability between the two reviewers for literature search, kappa score for the

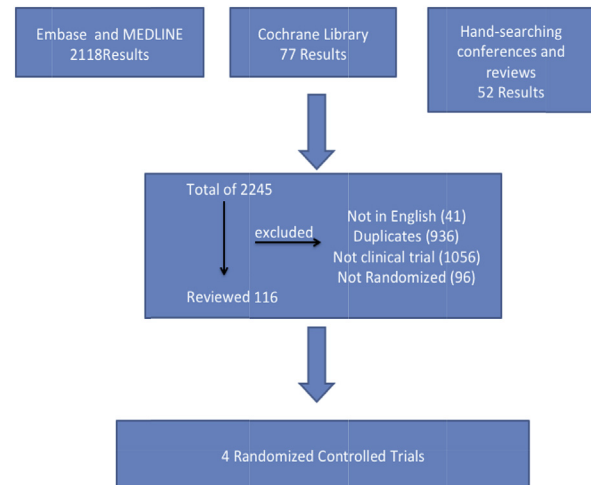


Fig 1. Literature research for selected studies.

included/excluded studies, data collection, and quality assessment was measured using kappa statistics and SPSS software (IBM, Armonk, NY). For dichotomous outcomes, risk ratio (RR) of open vs EVAR repair with confidence intervals (CIs) and *P* value are reported. Results were considered statistically significant at $P \leq .05$. Because of the possibility of a small number of studies and between-study heterogeneity, the pooled RR was calculated with the Mantel-Haenszel method for random effects.⁶ A random-effects model meta-analysis assumes that the true underlying effects vary between trials. An intention-to-treat analysis was performed by using the same end point definitions as in the primary studies. To assess heterogeneity across trials, we used the Cochrane χ^2 test based on the pooled RR. Heterogeneity was considered statistically significant at $P \leq .1$ because the heterogeneity test is underpowered when small numbers of studies are included. Also, the I^2 statistic was used to quantify heterogeneity; a value of <25% is considered small heterogeneity, a value of 25%-50% is considered as moderate heterogeneity, whereas a value >50% is considered as a large heterogeneity.⁶ Cochrane χ^2 statistic with *P* value and I^2 value are reported. A funnel plot is used to explore publication bias,⁶ but it is not recommended for less than 10 studies because asymmetry could appear because of chance.¹² Review Manager, v. 5.0 (Cochrane Collaboration, Copenhagen, Denmark), was used to generate the forest plots and RRs.

RESULTS

Our search identified 2245 abstracts. After review of the abstracts, we identified four randomized controlled trials that met our inclusion criteria (Fig 1). All were published within the past 4 years. All of the presented results in this study summarize the findings from the RCTs. None of the studies was blinded.

The Cohen's κ scores for the interobserver reliabilities for the literature search process and quality assessment are

Table II. The assessment of risk of bias in the trials was based on sequence generation; allocation concealment; blinding of participants, personnel, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias such as baseline imbalance, early stopping bias, academic bias, and source of funding bias

Bias	DREAM	EVAR 1	OVER	ACE
Sequence generation	Low	Moderate	Moderate	High
Allocation concealment	Low	Low	Low	Low
Blinding participants and personnel	Moderate-high	Moderate-high	Moderate-high	Moderate-high
Blinding outcome assessment	Moderate-high	Moderate-high	Moderate-high	Moderate-high
Incomplete outcome data	Low	Low	Low	High
Selective outcome reporting	Low	Low	Low	Low
Other sources	Moderate	Low	Low	Low

ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR 1, United Kingdom Endovascular Aneurysm Repair 1; OVER, Open Versus Endovascular Repair.

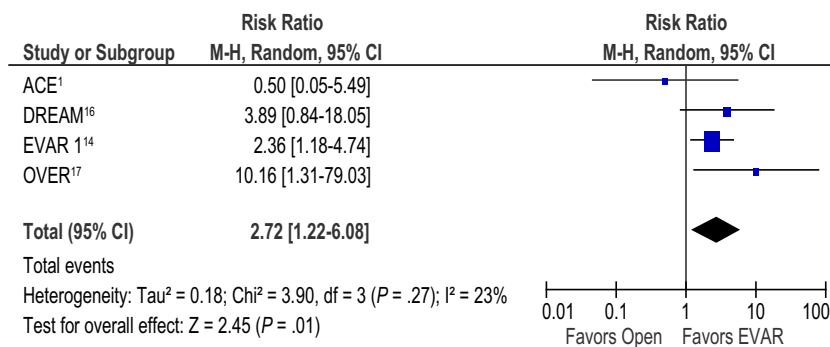


Fig 2. Forest plot of randomized trials comparing 30-day mortality rate after endovascular aneurysm repair (EVAR) and open repair of unruptured abdominal aortic aneurysms (AAAs). Endovascular in comparison to open repair has a lower 30-day postoperative all-cause mortality. ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; CI, confidence interval; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR 1, United Kingdom Endovascular Aneurysm Repair 1; OVER, Open Versus Endovascular Repair.

0.88, and 0.9, respectively. The data harvest level of agreement among M.Q. and F.P. varied from 83% to 100%.

The literature review also yielded a study by P. W. M. Cuypers et al 2001.¹³ However, we have decided not to include this study in the calculations that are presented. This article did not elicit the data necessary for our systematic review. The only outcome measure presented was short-term all-cause mortality. The mortality was not subdivided by cause, which makes it difficult to compare with the other studies included in this meta-analysis. To determine if the exclusion of this study skews the results, short-term mortality and all-cause mortality were calculated including this study. The results showed that the inclusion or exclusion of this study did not alter the overall outcome (data not shown).

Our literature review identified four trials that are used in our analysis. These studies reported outcomes of open repair vs EVAR repair of AAAs in patients who were candidates for both procedures (n = 2783).^{1,14-17} Table II summarizes the characteristics of the four RCTs that evaluated AAA repair. Sample size varied from 298 to 1252 with a similar number of participants in study groups. The mean age varied from 69 to 74 years, but it was similar between the groups for all studies. The mean follow-up time varied

from 2 years (United Kingdom Endovascular Aneurysm Repair 1 [EVAR 1], 2011) to 8 years (Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse [ACE], 2011), but all reported 30-day mortality as short term. The loss to follow-up for the ACE, Dutch Randomized Endovascular Aneurysm Repair (DREAM), EVAR 1, and Open Versus Endovascular Repair (OVER) studies was small: 8, 0, 17, and 2 patients, respectively.

Fig 2 shows a significant increased 30-day postoperative all-cause mortality in open repair compared with EVAR repair (3.2% vs 1.2%; RR, 2.81; 95% CI, 1.60-4.94). Findings were consistent across the studies. The between-study heterogeneity was of small size (I² = 23%). We also compared the long-term all-cause mortality between open and EVAR repair. As shown in Fig 3, there is no statistically significant difference in the long-term all-cause mortality between open and EVAR repair. RR was 0.95 (95% CI, 0.84-1.10) with no heterogeneity.

A comparison of reintervention rates in both groups was conducted and summarized in Fig 4. Although there was no statistical difference in the long-term all-cause mortality, it is shown in Fig 4 that reintervention procedures in the open repair group were 50% lower than in the EVAR repair group (9.3% vs 18.9%; RR, 0.49; 95%

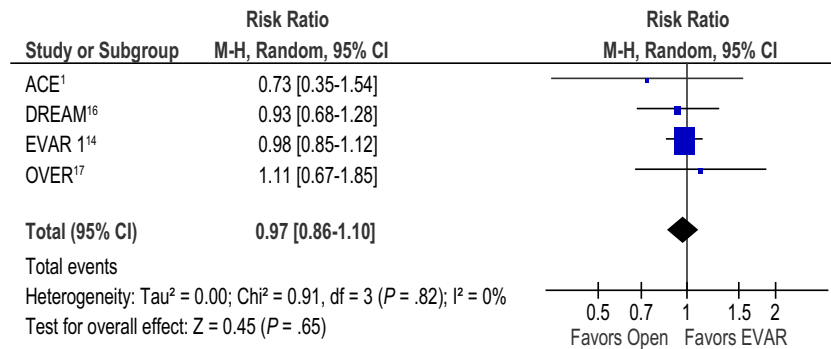


Fig 3. Forest plot of randomized trials comparing long-term mortality rate after endovascular aneurysm repair (EVAR) and open repair of unruptured abdominal aortic aneurysms (AAAs). There was no statistical difference in long-term all-cause mortality between endovascular and open repair of AAAs. ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; CI, confidence interval; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR 1, United Kingdom Endovascular Aneurysm Repair 1; OVER, Open Versus Endovascular Repair.

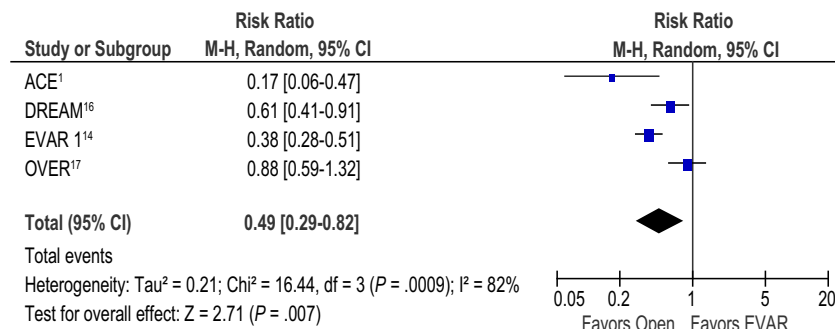


Fig 4. Forest plot of randomized trials comparing reintervention rates after endovascular aneurysm repair (EVAR) or open repair of unruptured abdominal aortic aneurysms (AAAs). Open in comparison to endovascular repair has a lower reintervention rate. ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; CI, confidence interval; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR 1, United Kingdom Endovascular Aneurysm Repair 1; OVER, Open Versus Endovascular Repair.

CI, 0.40-0.60). However, the large between-study heterogeneity of 82% undermines the validity of pooled RR for reintervention.

The long-term mortality was further divided by cause (cardiovascular, aneurysm related and stroke), and these were compared in both groups. Fig 5, A-C demonstrate no statistical difference in long-term mortality rates due to CVD, aneurysm related and stroke after EVAR or open repair of AAAs. CVD (RR, 0.9; 95% CI, 0.6-1.2) and stroke (RR, 0.9; 95% CI, 0.5-1.6) were in favor of open repair, but aneurysm-related deaths were (RR, 1.1; 95% CI, 0.5-2.5) were in favor of EVAR repair. Heterogeneity ($I^2 = 47\%$) of close to moderate size was present for aneurysm-related deaths that might be attributable to the small number of events in ACE 2011 and DREAM 2010 trials.

We have also refined our literature search to include nonrandomized prospective studies that compared the short- and long-term mortality events post-EVAR and open repair of AAAs.¹⁸⁻²³ Unlike the results we obtained

from RCT studies, the analysis of the prospective studies showed no statistical difference in the short-term all-cause mortality between open repair and EVAR repair (RR, 1.66; 95% CI, 1.05-2.62). The results from the long-term all-cause mortality from prospective cohort studies were not reliable because of the large between-study heterogeneity (80%). Hatala et al²⁴ recommended not to pool the results when heterogeneity is larger than 50%. The analysis of the prospective cohort studies showed no statistical difference in the long-term all-cause mortality between open repair and EVAR repair (RR, 0.75; 95% CI, 0.53, 1.06).

DISCUSSION

These results represent an up-to-date meta-analysis of the randomized trials for comparing open vs EVAR repair of AAAs. Open repair has long been accepted as the gold standard repair for AAAs because of its acceptable low risk, predictability for expected outcomes, and durability. EVAR has been established to help reduce short-term

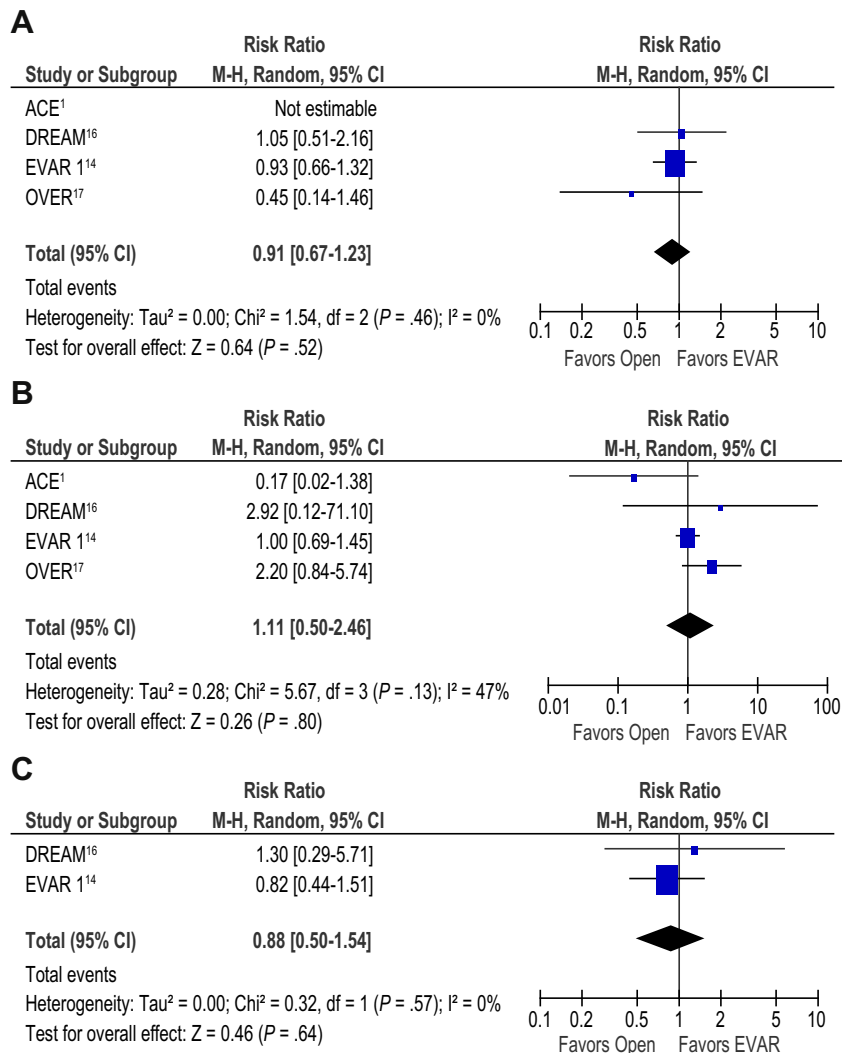


Fig 5. Forest plot of randomized trials comparing long-term mortality rates due to cardiovascular disease (CVD) (A), aneurysm related (B), and stroke (C) after endovascular aneurysm repair (EVAR) or open repair of unruptured abdominal aortic aneurysms (AAAs), respectively. There is no statistical difference in long-term mortality rates because of CVD, aneurysm related and stroke after EVAR, or open repair of AAAs. ACE, Anévrisme de L'aorte Abdominale: Chirurgie versus Endoprothèse; CI, confidence interval; DREAM, Dutch Randomized Endovascular Aneurysm Repair; EVAR 1, United Kingdom Endovascular Aneurysm Repair 1; OVER, Open Versus Endovascular Repair.

mortality associated with elective AAA repair.¹⁷ These initial benefits of EVAR, though, are not sustained on longer-term follow-up as confirmed with the EVAR 1, DREAM, and OVER trials as shown in this current meta-analysis. The French ACE trial found different results when it came to perioperative outcomes, as no early survival advantage was attributed to EVAR compared with open repair. They also found that in low-risk patients, open repair was as safe as EVAR, but with less reinterventions.

As demonstrated on most of the trials, the reintervention rate was higher in the EVAR group of patients. The DREAM and OVER trials appear to have counted reintervention rates for open and EVAR patients as graft-related

indications, wound-related indications (incisional hernia and wound infection), and local or systemic indications (bleeding, endoleak, and small bowel obstructions). The EVAR 1 and ACE trials appear to have counted reintervention rates for open and EVAR patients as graft-related interventions including graft rupture, endoleak, para-anastomotic aneurysm, graft replacement, and graft occlusions/stenoses. The lifetime need for reintervention in patients who undergo an EVAR repair approaches 20%. The OVER trial, though, considered more specifically surgical complications than both the DREAM and EVAR 1 trials and recorded a 5% rate of patients needing incisional hernia repairs. As such, OVER did not demonstrate a difference for reintervention rate between the types of repair. In

the ACE trial, there was a statistically significant difference when it came to wound complications between the open surgical repair and EVAR arms with 25% of patients undergoing open repair having complications vs 0.7% in the EVAR group. The ACE trial lists did not specifically record the incidence of abdominal wall reconstruction or incisional repairs following open repair group. The incidence of bowel obstruction associated with open surgery was also not reported. This may have affected the outcomes of their stated reintervention rate, such as with the OVER trial, as we know that incisional complications following open repair for AAA are not negligible.²⁵ The weight of the ACE trial, though, did not bear out in the Forest plot to affect the overall swing toward EVAR as requiring a higher rate of reintervention. This trend is also echoed in the EUROSTAR registry in which there was an overall 14% reintervention rate, with complications occurring more frequently in AAAs >5.5 cm.²⁶ In this current meta-analysis, we found a higher risk of reintervention for EVAR compared with open repair. However, the large heterogeneity between studies undermines the validity of the pooled RR for reintervention. This large heterogeneity might be due to the definition of and the reasons for reintervention that might differ from study to study.

In performing this meta-analysis, we were able to look at the current RCT literature for open vs EVAR repair as a whole. Any initial benefit that was gained with an EVAR approach was lost on longer-term follow-up in these studies. There is no statistical difference in the long-term mortality comparing open vs EVAR repair. This might be due to the fact that the length of follow-up varied between studies from 2 to 8 years.

Further study of long-term mortality by listed cause demonstrates no difference when comparing either CVD-related mortality, aneurysm-related mortality, or stroke-related mortality. This is not overly surprising, as those who survive the initial perioperative period often return back to their baseline risk, independent of type of procedure for AAA repair.

Based on this meta-analysis, we are able to demonstrate the short-term mortality benefits of an EVAR approach. For those patients with a life expectancy <2 years, an individualized treatment plan is prudent and thoughtful discussion with the patient in regard to overall goals of care should be had, based on the results of the EVAR 2 trial.²⁷ This group of patients that were deemed unfit to undergo open AAA repair were not included in our meta-analysis based on our inclusion criteria.

Although most patients in the DREAM, OVER, and EVAR 1 were fit for surgery, baseline characteristics may not be fully identical, and a similar distribution of risk factors does not fully take into account the association of risks. The OVER trial used the Research AND Development (RAND) surgical risk score with 53% patients considered as low risk for surgery. However, the risk assessment of patients in the EVAR 1 or DREAM was left to each center's appreciation. This difference in patient risk assessment may account for the heterogeneity in clinical findings

between the different studies. The ACE trial looked at patients who were low to moderate risk for undergoing surgical repair and excluded patients who had a life expectancy of less than 6 months, or were in category 3 of the Society for Vascular Surgery/American Association for Vascular Surgery comorbidity score for the clinical assessment. These differences might account for the between-study heterogeneity for 30-day postoperative mortality.

As with any meta-analysis, the results depend on the quality and quantity of the studies that were included in the analysis. Here, the four major randomized controlled trials for EVAR open repairs have been analyzed, as they met our search criteria. This includes over 2700 patients randomized. Other prospective studies were excluded, as they did not meet our full criteria of randomized trials or reporting of outcomes beyond 2 years. This does limit our breadth of studies captured but does help to create a clearer picture with similar patient groups. Although, as discussed in our Results section, the inclusion of a number of prospective nonrandomized trials reaffirms the long-term mortality equivalency of EVAR and open repairs, but also found a similar short-term equivalency. These results are interesting and confirm our data for long-term mortality. The difference in the short-term mortality between prospective studies and RCTs can be attributed to the lack of randomization and selection bias of patients. These studies might have recruited younger patients with few comorbidities who are better fit to undergo an open repair and the older patients, or those with more medical comorbidities to undergo an endovascular repair. Therefore, we must analyze the prospective studies with caution since they are prone to selection bias and information bias. Also, because of the lack of randomization, a higher potential for confounding factors can sometimes be observed in prospective studies.

The strength of this systematic review and meta-analysis is that any potential biases for search strategy, inclusion and exclusion of the studies, and data collection are minimized by an independent review process. Also, only randomized controlled trials are included, appropriate statistical methods are used and study heterogeneity is accounted for in the analysis. The weakness of this study is the small number of the included studies; we, however, ensured that all eligible studies were included and our separate analysis of nonrandomized prospective trials did not add much to the conclusions drawn.

CONCLUSIONS

Through this meta-analysis, we are able to confer with most recent studies on EVAR for AAAs. EVAR reduces the short-term mortality associated with surgical repair, but this benefit is not sustained on longer-term follow-up. It is also confirmed that the reintervention rate was higher with an EVAR repair. This is an up-to-date review of the most recent randomized controlled trials comparing open with EVAR repair for AAAs. This meta-analysis supports the notion of an endovascular-first approach to AAAs

attributable to the short-term benefit of EVAR and the long-term mortality equivalency.

AUTHOR CONTRIBUTIONS

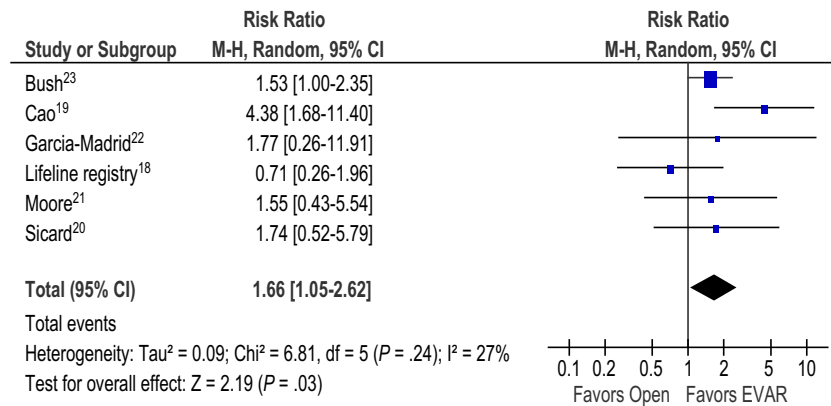
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Data collection: MQ, FP
Writing the article: MQ, FP, AA, FF, JH
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REFERENCES

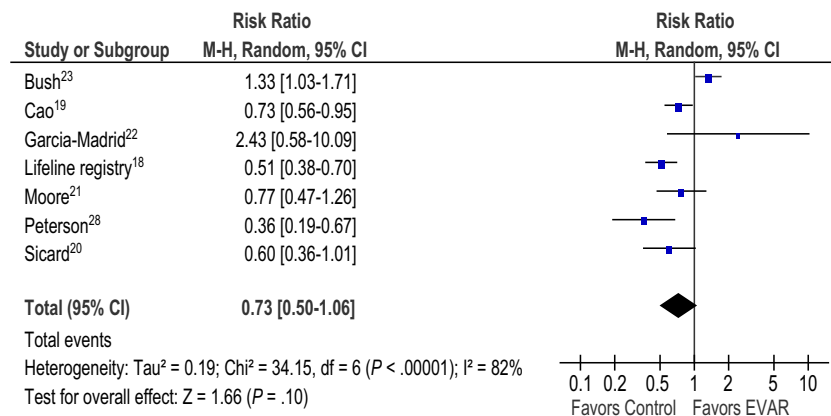
1. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysm in low-to-moderate-risk patients. *J Vasc Surg* 2011;53:1167-73.
2. Sakalihasan N, Limet R, Defaw OD. Abdominal aortic aneurysm. *Lancet* 2005;365:1577-89.
3. Kniemeyer HW, Kessler T, Reber PU, Ris HB, Hakki H, Widmer MK. Treatment of ruptured abdominal aortic aneurysm, a permanent challenge or a waste of resources? Prediction of outcome using a multi-organ-dysfunction score. *Eur J Vasc Endovasc Surg* 2000;19:190-6.
4. Eliason JL, Upchurch GR Jr. Endovascular abdominal aortic aneurysm repair. *Circulation* 2008;117:1738-44.
5. Sajid MS, Desai M, Haider Z, Baker DM, Hamilton G. Endovascular aortic aneurysm repair (EVAR) has significantly lower perioperative mortality in comparison to open repair: a systematic review. *Asian J Surg* 2008;31:119-23.
6. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions* 2011: Version 5.1.0. The Cochrane Collaboration. Available at: www.cochrane-handbook.org. Accessed March 2012.
7. Kjaergard LL, Villumsen J, Gluud C. Reported methodologic quality and discrepancies between large and small randomized trials in meta-analyses. *Ann Intern Med* 2001;135:982-9.
8. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet* 1998;352:609-13.
9. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;273:408-12.
10. Wood L, Egger M, Gluud LL, Schulz KF, Juni P, Altman DG, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;336:601-5.
11. Gluud C, Nikolova D, Klingenberg S, Alexakis N, Als-Nielsen B, D'Amico G, et al. Cochrane Hepato-Biliary Group. About the Cochrane Collaboration (Cochrane Review Groups [CRGs]). Chapter 8. Art. No. LIVER. 2008;4. Available at: http://www.mrw.interscience.wiley.com/cochrane/cochrane_clsystrev_crglist_fs.html. Accessed November 6, 2009.
12. Duval S, Tweedie R. Trim and fill: a simple funnel-plot based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455-63.
13. Cuypers PW, Gardien M, Buth J, Peels CH, Charbon JA, Hop WC. Randomized study comparing cardiac response in endovascular and open abdominal aortic aneurysm repair. *Brit J Surg* 2001;88:1059-65.
14. EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR Trial 1): randomised controlled trial. *Lancet* 2005;365:2179-86.
15. Brown LC, Thompson SG, Greenhalgh RM, Powell JT. Incidence of cardiovascular events and death after open or endovascular repair of abdominal aortic aneurysm in the randomized EVAR trial 1. *Brit J Surg* 2011;98:935-42.
16. De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven E, Cuypers P, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010;362:1881-9.
17. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT Jr, Matsumura JS, Kohler TR, et al. Open Versus Endovascular Repair (OVER) Veterans Affairs Cooperative Study Group. *JAMA* 2009;302:1535-42.
18. Lifeline Registry of EVAR Publications Committee. Lifeline registry of endovascular aneurysm repair: long-term primary outcome measures. *J Vasc Surg* 2005;42:1-10.
19. Cao P, Verzini F, Parlani G, Romano L, De Rango P, Pagliuca V, et al. Clinical effect of abdominal aortic aneurysm endografting: 7-year concurrent comparison with open repair. *J Vasc Surg* 2004;40:841-8.
20. Sicard GA, Zwolak RM, Sidawy AN, White RA, Siami FS. Endovascular abdominal aortic aneurysm repair: long-term outcome measures in patients at high-risk for open surgery. *J Vasc Surg* 2006;44:229-36.
21. Moore WS, Matsumura JS, Makaroun MS, Katzen BT, Deaton DH, Decker M, et al. Five-year interim comparison of the Guidant bifurcated endograft with open repair of abdominal aortic aneurysm. *J Vasc Surg* 2003;38:46-55.
22. Garcia-Madrid C, Josa M, Rimbau V, Mestres CA, Muntana J, Mulet J. Endovascular versus open surgical repair of abdominal aortic aneurysm: a comparison of early and intermediate results in patients suitable for both techniques. *Eur J Vasc Endovasc Surg* 2004;28:365-72.
23. Bush RL, Johnson ML, Hedayati N, Henderson WG, Lin PH, Lumsden AB. Performance of endovascular aortic aneurysm repair in high-risk patients: results from the Veterans Affairs National Surgical Quality Improvement Program. *J Vasc Surg* 2007;45:227-33; discussion: 233-5.
24. Hatala R, Keitz S, Wyer P, Guyatt G. Tips for learners of evidence-based medicine: 4. Assessing heterogeneity of primary studies in systematic reviews and whether to combine their results. *CMAJ* 2005;172:661-5.
25. Raffetto JD, Cheung Y, Fisher JB, Cantelmo NL, Watkins MT, Lamorte WW, et al. Incision and abdominal wall hernias in patients with aneurysm or occlusive aortic disease. *J Vasc Surg* 2003;37:1150-4.
26. Leurs LJ, Buth J, Laheij RJ; EUROSTAR Collaborators. Long-term results of endovascular abdominal aortic aneurysm treatment with the first generation of commercially available stent grafts. *Arch Surg* 2007;142:33-41.
27. United Kingdom EVAR Trial Investigators. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010;362:1872-80.
28. Peterson BG, Matsumura JS, Brewster DC, Makaroun MS. Five-year report of a multicenter controlled clinical trial of open versus endovascular treatment of abdominal aortic aneurysms. *J Vasc Surg* 2007;45:885-90.

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Supplementary Fig 1 (online only). Forest plot of prospective studies comparing 30-day mortality rate after endovascular aneurysm repair (EVAR) and open repair of unruptured abdominal aortic aneurysms (AAAs). Endovascular and open repair had similar 30-day postoperative all-cause mortality. *CI*, Confidence interval.



Supplementary Fig 2 (online only). Forest plot of prospective studies comparing long-term mortality rate after endovascular aneurysm repair (EVAR) and open repair of unruptured abdominal aortic aneurysms (AAAs). There was no statistical difference in long-term all-cause mortality between endovascular and open repair of AAAs. *CI*, Confidence interval.